

WHAT IS CLAIMED IS:

1. A method for screening for a potential novel agent effective to inhibit the development of malignancies associated with a chronic viral infection, whereby said viral infection is caused by a virus which contains a viral protein with an interferon sensitivity determining region (ISDR), comprising:

incubating a mixture containing PKR protein kinase, the viral protein, and an agent to be tested, and measuring PKR protein kinase activity, comparing to PKR protein kinase activity in the absence of the agent to be tested, and identifying a potential agent by the indication of PKR protein kinase activity in the presence of a test agent.

2. The method of Claim 1 wherein the agent inhibits the malignancies associated with chronic hepatitis C viral infection.

3. The method of Claim 1 wherein the viral protein is NS5A.

4. A method for screening for a potential agent effective to inhibit the development of malignancies associated with a chronic viral infection, whereby said viral infection is caused by a virus which contains a viral protein with an interferon sensitivity determining region (ISDR), whereby said agent is effective in inhibiting the direct interaction of an ISDR containing viral protein with an interferon induced PKR kinase, comprising:

incubating a mixture containing the ISDR containing protein, PKR protein kinase and an agent to be tested, and measuring the binding of the ISDR containing protein and the PKR protein, comparing to the degree of binding in the absence of the agent to be tested, and identifying a potential agent by the indication of PKR protein kinase activity in the presence of a test agent.

5. The method of Claim 4 wherein the viral protein is NS5A.

6. The method of Claim 4 wherein the agent inhibits the malignancies associated with chronic hepatitis C viral infection.

7. The method of Claim 1, wherein the PKR protein kinase and the protein containing an ISDR are expressed in a yeast cell genetically engineered to increase expression of a reporter gene in the presence of activated PKR protein kinase, and further comprising measuring the level of expression of the reporter gene in the presence and absence of the agent to be tested.

8. The method of Claim 7, wherein the reporter gene product is fused to GCN4/ $\beta$ -gal protein.

9. A method for screening for agents comprising a yeast cell which is genetically engineered to express:

- (a) a polypeptide containing an ISDR region, and
- (b) an interferon-induced PKR protein kinase, and

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(c) a reporter gene whose expression is increased in response to activation of the PKR protein kinase, and further comprising measuring the level of expression of the reporter gene in the presence and absence of the agent to be tested.

10. The method of Claim 9 wherein the polypeptide containing an ISDR region is NS5A.

11. The method of Claim 10 wherein the reporter gene is a fused GCN4/ $\beta$ -gal gene.

12. A method of inhibiting the development of malignancies associated with chronic hepatitis C virus (HCV) infection in a cell infected with HCV, comprising administering an effective amount of an agent which interferes with the interaction between NS5A and PKR to said cell, said agent comprising an antisense molecule complementary to the ISDR.